

What is claimed is:

1. A microorganism comprising a regulated antigen delivery system (RADS), wherein the RADS comprises
- (a) a vector comprising (1) a site for insertion of a gene encoding a desired gene product; (2) a first origin of replication (ori) conferring vector replication using DNA polymerase III; and (3) a second ori conferring vector replication using DNA polymerase I, wherein the second ori is operably linked to a first control sequence repressible by a first repressor, and wherein the runaway vector does not comprise a phage lysis gene; and
- (b) a gene encoding a first repressor operably linked to a first activatable control sequence.
2. The microorganism of claim 1, further comprising a gene encoding a desired gene product inserted into the site of step (a), wherein the gene encoding the desired gene product is operably linked to a second control sequence.
3. The microorganism of claim 2, wherein the first control sequence and the second control sequence are the same sequence.
4. The microorganism of claim 2, wherein the first control sequence and the second control sequence are different sequences.
5. The microorganism of claim 1, wherein the repressor is selected from the group consisting of LacI repressor and C2 repressor, and wherein the second control sequence is repressible by a second repressor.
6. The microorganism of claim 2, wherein
- (a) the vector is a plasmid,
- (b) the desired gene product is an antigen and
- (c) the microorganism is an attenuated derivative of a pathogenic bacterium
7. The microorganism of claim 6, wherein the microorganism is a *Salmonella* sp.
8. The microorganism of claim 6, wherein the first activatable control sequence is *araCP<sub>BAD</sub>*.

9. The microorganism of claim 6, further comprising a balanced lethal host-vector system consisting of a lack of a functioning essential gene on the chromosome and a recombinant functioning copy of the essential gene on the vector.

10. The microorganism of claim 9, wherein the essential gene is an *asd* gene.

11. The microorganism of claim 10, wherein the *asd* gene is inactivated by the insertion of a repressor gene operably linked to *araCP<sub>BAD</sub>*.

12. The microorganism of claim 6, further comprising an inactivating mutation in a native gene selected from the group consisting of *cya*, *crp*, *phoPQ*, *ompR*, *galE*, *cdt*, *hemA*, *aroA*, *aroC*, *aroD* and *htrA*.

13. The microorganism of claim 6, wherein the first ori is a pSC ori, and the second ori is a pUC ori

14. The microorganism of claim 6, wherein the first control sequence is P22 P<sub>R</sub> and the first repressor is C2 repressor.

15. The microorganism of claim 6, wherein the second control sequence is P<sub>trc</sub> and wherein the second control sequence is repressible by a second repressor, and wherein the second repressor is a LacI repressor.

16. The microorganism of claim 15, wherein the first control sequence is P22 P<sub>R</sub>; the first repressor is C2 repressor; the first ori is a pSC ori, and the second ori is a pUC ori.

17. The microorganism of claim 16, wherein the vector is pMEG-771, or modifications thereof, with a gene encoding an antigen.

18. The microorganism of claim 6, wherein the antigen is selected from the group consisting of Ery65 and SeM.

19. The microorganism of claim 6, wherein the desired gene product is operably linked to a eukaryotic control sequence.

20. The microorganism of claim 19, further comprising a  $\Delta endA$  mutation.

21. A runaway vector comprising the vector in the microorganism of claim 19.

22. The microorganism of claim 6, which exhibits delayed RADS characteristics, wherein the delayed RADS characteristics are conferred by an alteration selected from the group consisting of: mutations that delay the loss of activator molecules by metabolism and/or leakage, a mutation or insertion to increase repressor concentration, and inclusion of a vector control sequence with binding sites for more than one repressor and/or vector sequences encoding repressor molecules that act on a vector control sequence.

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23. A method of producing a desired gene product, comprising, in order,

(a) engineering a gene encoding the desired gene product into the vector in the microorganism of claim 6, wherein the microorganism comprises control sequences that repress expression of the second ori under a first environmental condition, but in which the expression of the second ori is derepressed under a second environmental condition;

5 (b) culturing the microorganism of step (a) under the first environmental condition; and

(c) culturing the microorganism with runaway vector of step (a) under the second environmental condition for a time sufficient to produce the desired gene product.

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24. The method of claim 23, wherein the desired gene product is an antigen.

25. The method of claim 24, wherein the first environmental condition comprises the presence of arabinose and the second environmental condition comprises the absence of arabinose.

26. The method of claim 25, wherein the first environmental condition comprises *in vitro* culture conditions and the second environmental condition comprises conditions inside of a vertebrate.

27. The method of claim 26, wherein

(a) the first ori is a pSC ori;

(b) the second ori is a pUC ori, which is operably linked to a repressing control sequence consisting of P22 P<sub>R</sub>;

- 5 (c) the product control sequence is  $P_{trc}$ ;
- (d) the microorganism comprises a gene encoding a first repressor operably linked to a first activatable control sequence, wherein the first repressor is C2; and
- (e) the microorganism comprises a gene encoding a second repressor operably linked to a second activatable control sequence, wherein the second repressor is
- 10 LacI;
- (f) the microorganism comprises a chromosome without a functional *asd* gene and the runaway vector comprises a functional *asd* gene; and
- (g) the microorganism comprises an inactivating mutation in a native gene selected from the group consisting of *cya*, *crp*, *phoPQ*, *ompR*, *galE*, *cdt*, *hemA*, *aroA*, *aroC*,  
15 *aroD* and *htr*.

28. The method of claim 27, wherein the first environmental condition comprises the presence of arabinose and the second environmental condition comprises the absence of arabinose.

29. The method of claim 28, wherein the microorganism further comprises an inactivating deletion in the *araCBAD* operon and/or the *araE* gene.

30. The method of claim 29, wherein the desired gene product is selected from the group consisting of Ery65 and SeM.

31. The method of claim 29, wherein the desired gene product is operably linked to a eukaryotic control sequence.

32. A vaccine for immunization of a vertebrate, the vaccine comprising the microorganism of claim 6 in a pharmaceutically acceptable carrier.

33. The vaccine of claim 32, wherein the microorganism is a *Salmonella sp.*

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34. The vaccine of claim 32, wherein:
- (a) the first ori is a pSC ori;
- (b) the second ori is a pUC ori, which is operably linked to a repressing control sequence consisting of P22  $P_R$ ;
- 5 (c) the product control sequence is  $P_{trc}$ ;

- (d) a gene encoding a first repressor operably linked to a first inducible control sequence, wherein the first repressor is C2; and
- (e) a gene encoding a second repressor operably linked to a second inducible control sequence, wherein the second repressor is LacI.

35. The vaccine of claim 34, wherein the first activatable control sequence and the second inducible control sequence are both *araCP<sub>BAD</sub>*.

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36. The vaccine of claim 35, wherein the microorganism further comprises an inactivating deletion in the *araCBAD* operon and or the *araE* gene.

37. A method of inducing immunoprotection in a vertebrate comprising administering the vaccine of claim 32 to the vertebrate.

38. A method of delivering a desired gene product to a vertebrate comprising administering the microorganism of claim 1 to the vertebrate.